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# Effect of ambient air pollution during pregnancy on preterm births: time-to-event analysis in Kampala City, Uganda, October 2021– September 2022

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# Summary

**Introduction**: Gestational exposure to fine particulate matter (PM<sub>2.5</sub>) has been associated with adverse birth outcomes. We investigated the effect of gestational PM<sub>2.5</sub> exposure on preterm birth (PTB) in Kampala City, October 2021–September 2022.

Methods: We conducted a retrospective cohort study among mothers with singleton pregnancies ≥28 weeks of gestation who resided in Kampala City throughout their pregnancy, and delivered at Kawempe National Referral Hospital. PTB was defined as delivery before 37 weeks from first day of the last menstruation period. We estimated gestational PM<sub>2.5</sub> exposure based on average PM<sub>2.5</sub> concentration obtained from the nearest Clarity© Node Solar–Powered monitor to the primary residence during pregnancy. We applied Mann Whitney U test to compare gestational PM<sub>2.5</sub> exposure between pregnant mothers who had PTB and term birth. Gestational exposure to PM<sub>2.5</sub> concentration was considered as the principal predictor of PTB, and we subsequently adjusted for potential covariates using multivariate regression with the Cox proportional hazards model. We assessed statistical significance of the multiplicative interaction by antepartum complications using Wald's Chi-squared test.

**Results**: Among 1,540 births, 229 (15%) were preterm. Overall, average gestational PM<sub>2.5</sub> exposure was  $66\mu g/m^3$  (range:  $45-75\mu g/m^3$ ). Significant difference in gestational PM<sub>2.5</sub> exposure was observed between pregnant mothers who had preterm birth and those who delivered at term (p=0.002). For every unit increase in average gestational PM<sub>2.5</sub> exposure, risk of incidence of preterm birth increased by 3% (HR=1.03, 95%CI: 1.01–1.05). Pregnant mothers who developed hypertensive disorders had 61% (HR=1.61, 95%CI: 1.05–2.48) higher risk of experiencing PTB compared to their counterparts. There was no statistically significant difference in stratum specific hazard ratios between gestational PM<sub>2.5</sub> exposure and incidence of preterm birth by antepartum complications.

**Conclusion**: We observed significant impact of PM<sub>2.5</sub> concentration on incidence of PTB in Kampala City. Efforts aimed at reducing preterm births should also prioritize mitigation of air pollution to improve maternal and child health.



Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1



#### Background

Fine particulate matter (PM<sub>2.5</sub>) is among the health-damaging air pollutants that pose adverse risks to humans due to its small size and diameter: which easily permit penetration into invasive systems [1]. PM<sub>2.5</sub> has been recommended as the best measure of air guality due to its prevalence in the environment and broad range of health effects with levels >15 µg/m<sup>3</sup> being associated with adverse consequences. Gestational exposure to PM2.5 increases the risks for preterm birth, defined as delivery before 37 weeks or 259 days from the first day of a pregnant woman's last menstruation to delivery. Preterm birth is categorized into extremely preterm birth (<28 weeks), very preterm birth (28 to <32 weeks), and moderate preterm birth (32 to <37 weeks). Preterm births have been substantially linked to an increase in neonatal and infant mortality and development of chronic physical and neurological morbidity among the survivors compared to term births. The prevalence of preterm birth attributed to gestational PM<sub>2.5</sub> exposure ranges from 12% to 24% worldwide [2]. A study conducted in Africa found a significant association between gestational exposure to PM2.5 and the incidence of preterm birth with an odds ratio of 1.08 (95% CI: 1.01, 1.16) [3]. Despite the fact that the direct causative mechanism is unknown, it is hypothesized that PM<sub>2.5</sub> affects transplacental oxygen and nutrient transport thus placental inflammation, oxidative stress, and blood coagulation which may limit intrauterine fetal growth.

Cities are more prone to poor air quality compared to non-urban areas. This is attributed to high population density, exhaust emissions from vehicles and industries, infrastructure construction, open fuel and solid waste burning. As of 2021, Kampala City was among the cities with the highest levels of PM<sub>2.5</sub>, exceeding the annual WHO recommended air quality PM<sub>2.5</sub> levels by 5 to 7 times. [4]. However, limited evidence has been presented about the association between PM<sub>2.5</sub> exposure and preterm births in this city. Understanding the impact of air quality on the incidence of preterm births would be a great initiative towards influencing the implementation of evidence-based air quality control strategies that address adverse birth outcomes. We investigated the impact of PM<sub>2.5</sub> exposure during pregnancy on preterm birth (PTB) in Kampala City, Uganda, October 2021–September 2022.

# Methods

# Study setting

This assessment was conducted in Kampala, the capital city of Uganda. It is divided into 5 administrative divisions: Central, Kawempe, Makindye, Rubaga, and Nakawa. The city has a surface area of 189 km<sup>2</sup>, including 176 km<sup>2</sup> of land and 13 km<sup>2</sup> of water [5]. The 2023 population was estimated at 1.76 million; however, the city has a dynamic and transient day population estimated at 5 million people [6]. Kampala Capital City Authority (KCCA) has been mandated to govern and administer Kampala Capital City on behalf of the Central Government of Uganda. Kawempe National Referral Hospital (KNRH), located about 12km away from the city centre of Kampala, is a government-funded hospital largely providing free maternal and newborn healthcare services to patients referred from public and private health facilities within and outside Kampala City, as well as walk-ins from Kampala Metropolitan Area and surrounding districts. KNRH is serving a population of approximately 4.5 million [7]. The catchment area of the hospital has a heterogeneous population, consisting of the urban poor and those with average income. In 2019, 2,784 (11%) out of 24,526 deliveries were preterm based on KNRH records [8].



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Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1

## Study design, population, exclusion criteria, and sample size considerations

We conducted a retrospective cohort study among mothers who delivered at KNRH. Mothers with viable pregnancies of at least 28 weeks of gestation who delivered from the labour suite or theatre between October 1, 2021, and September 30, 2022, were identified to define our population-based birth cohort (n=22,192). Mothers whose weeks of gestation at birth or the first day of the last normal menstrual period were not documented in the file were excluded. Furthermore, all mothers whose first day of the last normal menstrual period occurred before October 1, 2021, were excluded to ensure that the exposure period accommodates all the weeks of gestation. Every mother with a valid telephone contact was reached out to confirm whether she resided in Kampala City, and then specify the division, parish, and duration of residence during pregnancy. Only 1,540 mothers who resided in Kampala City throughout their pregnancy time were enrolled in this assessment.

# Study variables and data abstraction Covariates

We abstracted data regarding the covariates from the mother's files using a data abstraction tool deployed in Kobo Collet. We considered the following potential individual covariates: demographic characteristics (maternal age, highest education level, marital status, occupation, HIV status), antenatal attendance, number of antenatal visits, history of smoking and alcohol use, and antepartum obstetric complications (eclampsia, pre-eclampsia, placenta abruptio, placenta previa, intra uterine fetal death (IUFD), preterm premature rupture of membranes, chorioamnionitis, and oligohydramnios). Only primary antepartum complications were considered for mothers who had multiple complications. Eclampsia and pre-eclampsia were categorized under hypertensive disorders. Placenta abruption and placenta previa were categorized under antepartum hemorrhage. Information on any covariates with missing data were obtained through telephone interviews with the mothers.

#### Gestational PM<sub>2.5</sub> exposure

In December 2019, KCCA installed twenty–four Clarity© Node Solar–Powered monitors for outdoor air quality monitoring in all five divisions of Kampala City (Figure 1). Clarity© Node Solar–Powered monitors were permanently set up at least 1.5 meters above ground level in secure areas away from obstruction or emission sources that could interfere with air quality measurements. Calibration of Clarity© Node Solar–Powered monitors was based on co–location data with the reference air quality monitoring station at the US Embassy in Kampala City. Clarity© Node Solar–Powered monitors use inbuilt cellular connectivity to transmit raw data for PM<sub>2.5</sub>, PM<sub>10</sub>, nitrogen dioxide (NO<sub>2</sub>), temperature, and relative humidity. Calibrated data generated by these monitors are accessed in real–time on the Clarity© Dashboard by authorized KCCA staff and Clarity© operating team.



**Quarterly Epidemiological Bulletin: July-September, 2023** 



Volume 8 / Issue 3 /Article No. 1



Figure 1: Location of Clarity© Node Solar–Powered monitors in Kampala City, Uganda

We abstracted 24–hour average PM<sub>2.5</sub> concentrations generated by calibrated Clarity© Node Solar– Powered monitors from the Clarity© Dashboard from October 1, 2021, to September 30, 2022. For each mother, the centroid coordinates for the respective parish of residence in Kampala City was obtained from the geo-spatial database for Kampala City. The distance between parish coordinates and coordinates for all the Clarity Node Solar-Powered monitors installed in the city was calculated. The nearest Clarity Node Solar-Powered monitor to the parish of the mother was determined based on the least distance obtained. We estimated PM<sub>2.5</sub> exposure during pregnancy based on average PM<sub>2.5</sub> concentration obtained from the nearest Clarity© Node Solar–Powered monitor throughout the gestation period.



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Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1

# Outcome variable

Our outcome variable was preterm birth, defined as delivery before 37 weeks or 259 days from the first day of a pregnant woman's last menstruation to delivery. Preterm birth was categorized into extremely very preterm birth (28 to <32 weeks) and moderate preterm birth (32 to <37 weeks) [9, 10]. Weeks of gestation were determined following standard obstetric practice based on first day of the last normal menstrual period or obtained from the ultrasound scan done during the first trimester for mothers who did not recall their first day of the last normal menstrual period.

# Data analysis

Descriptive statistics were performed for demographic characteristics, antenatal attendance, and antepartum complications. We computed the incidence of preterm births (28<37 weeks) and further stratified into extremely very preterm birth (28 to <32 weeks) and moderate preterm birth (32 to <37 weeks). We calculated gestational PM<sub>2.5</sub> exposure among pregnant mothers who experienced preterm birth (28<37 weeks) and term birth (≥37 weeks). We applied Mann Whitney U test to compare gestational PM<sub>2.5</sub> exposure between pregnant mothers who experienced preterm birth and term birth. Gestational exposure to PM<sub>2.5</sub> concentration was considered as the principal predictor of PTB. Due to variability in the exposure length (weeks of gestation) for each birth, we utilized the Cox proportional hazards models based on weeks of gestation to determine the association between gestational PM<sub>2.5</sub> exposure over the entire pregnancy and the risk of preterm birth. We subsequently adjusted for potential covariates using multivariate regression with the Cox proportional hazards model to obtain adjusted hazard ratios (HR), corresponding 95% confidence intervals and p-values. We stratified data by each covariate to generate stratum-specific hazard ratios between gestational PM<sub>2.5</sub> exposure and preterm birth. To assess whether antepartum complications modified the relationship between gestational PM<sub>2.5</sub> concentration and preterm birth, we generated interaction terms between gestational PM<sub>2.5</sub> concentration and antepartum complications. Interpretation of the interaction term's hazard ratios and respective statistical significance explained whether the effect of gestational PM<sub>2.5</sub> concentration on preterm birth varied by the presence or absence of the antepartum complications. We used the Wald's Chi-squared test to assess the statistical significance of the multiplicative interaction between gestational PM<sub>2.5</sub> exposure and antepartum complications. Statistical significance was set at a p-value < 0.05. All statistical analyses were performed using STATA 16.0.

# **Ethical considerations**

The Office of the Associate Director for Science, US Centres of Disease Control and Prevention/Uganda, also determined that this activity was not human subject research, and its primary intent was public health practice or a disease control activity (specifically, epidemic or endemic disease control activity). Administrative clearance to extract data from patient files and PM<sub>2.5</sub> exposure data from the Clarity© Dashboard was obtained from Kawempe National Referral Hospital and Kampala Capital City Authority respectively. All methods were performed in accordance with the approval and administrative clearance. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy. §

<sup>§</sup>See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.



Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1



#### Results

Characteristics of study participants during an evaluation of gestational PM<sub>2.5</sub> exposure on preterm births in Kampala City, Uganda, October 2021–September 2022

Out of 1,540 pregnant mothers, 1,030 (66.9%) were aged 18–29 and 892 (57.9%) were housewives. Of note, only 819 (53.2%) attended antenatal care. Only 382 (24.8%) had antenatal obstetric complications (Table 1).

 Table 1: Characteristics of study participants during an evaluation of gestational PM2.5

 exposure on preterm births in Kampala City, Uganda, October 2021–September 2022

Study variables	Frequencies (n=1,540)	<sup>s</sup> Percentages (%)	
Completed age			
Below 18	53	3.4	
18–29	1,030	66.9	
30–39	419	27.2	
40–49	38	2.5	
Division of residence			
Kawempe	466	30.3	
Makindye	336	21.8	
Nakawa	105	6.8	
Rubaga	428	27.8	
Central	205	13.3	
Highest education level			
None	412	26.8	
Primary	346	22.5	
Secondary	515	33.4	
Tertiary or above	267	17.3	
Marital Status			
Not Married	236	15.3	
Married	1,304	84.7	
Occupation			
House wife	892	57.9	
Formal employment	156	10.1	
Business	492	32.0	
Number of children			
1 – 2	931	60.5	
3 – 4	447	29.0	
5 and above	162	10.5	
HIV status			
Negative	1,412	91.7	
Positive	107	6.9	
Unknown	21	1.4	
Antenatal attendance			
No	721	46.8	
Yes	819	53.2	



Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1



Number of antenatal visits (n=819)					
1 – 2	111	13.6			
3 – 4	401	48.9			
5 and above	307	37.5			
History of smoking					
No	1,523	98.9			
Yes	17	1.1			
History of alcohol use					
No	1,512	98.2			
Yes	28	1.8			
Antenatal obstetric complication					
No	1,158	75.2			
Yes	382	24.8			
Preterm premature rupture of membranes					
No	1,436	93.2			
Yes	104	6.8			
Hypertensive disorder					
No	1,431	92.9			
Yes	109	7.1			
Antepartum hemorrhage					
No	1,484	96.4			
Yes	56	3.6			
Oligohydramnios					
No	1,495	97.1			
Yes	45	2.9			
Chorioamnionitis					
No	1,493	97.0			
Yes	47	3.0			
Intra uterine fetal death (IUFD)					
No	1,519	98.6			
Yes	21	1.4			

#### Incidence of preterm births in Kampala City, Uganda, October 2021–September 2022

Among pregnant mothers who resided in Kampala City throughout pregnancy and delivered from KNRH, 229 (14.9%) had preterm births (Table 2). Of these, the majority, 198 (86.5%) had moderate to late preterm births whereas only 31 (13.5%) had very preterm births.

#### Gestational PM<sub>2.5</sub> exposure

Overall, the average gestational  $PM_{2.5}$  exposure was  $66\mu g/m^3$  (range:  $45-75\mu g/m^3$ ). Gestational  $PM_{2.5}$  exposure was slightly higher among pregnant mothers who experienced preterm birth compared to those who delivered at term (Table 2). Significant difference in gestational  $PM_{2.5}$  exposure was observed between pregnant mothers who experienced preterm birth and those who delivered at term (p=0.002).

#### Factors associated with incidence of preterm births in Kampala City, Uganda, October 2021– September 2022



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Volume 8 / Issue 3 /Article No. 1

At multivariate analysis, gestational PM<sub>2.5</sub> exposure and development of hypertensive disorders were statistically significantly associated with incidence of preterm births among pregnant mothers in Kampala City. For every unit increase in average PM<sub>2.5</sub> exposure during pregnancy, the risk of incidence of a preterm birth increases by 3% (HR=1.03 [1.01 – 1.05]). Pregnant mothers who developed hypertensive disorders were 61% more likely to have preterm births compared to those who did not develop hypertensive disorders during pregnancy (HR=1.61 [1.05 – 2.48]) (Table 2).

Table 2: Factors associated with incidence of preterm births in Kampala City, Uganda, October	
2021–September 2022	

Study variables	Term birth	Preterm birth	Adjusted	95% confidence
	n (%)	n (%)	hazard ratios	intervals
Socio-demographic charact	teristics			
Completed age				
Below 18	43 (3.3)	10 (4.4)	Ref.	
18–29	879 (67.0)	151 (65.9)	0.63	[0.33 – 1.21]
30–39	358 (27.3)	61 (26.6)	0.59	[0.29 – 1.17]
40–49	31 (2.4)	7 (3.1)	0.79	[0.30 - 2.09]
Highest education level				
None	348 (26.5)	64 (27.9)	Ref.	
Primary	297 (22.7)	49 (21.4)	0.86	[0.58 – 1.25]
Secondary	440 (33.6)	75 (32.8)	0.91	[0.64 – 1.28]
Tertiary or above	226 (17.2)	41 (17.9)	0.92	[0.61 – 1.40]
Marital Status				
Married	1,118 (85.3)	186 (81.2)	Ref.	
Not married	193 (14.7)	43 (18.8)	1.31	[0.92 – 1.86]
Occupation				
House wife	761 (58.0)	131 (57.2)	Ref.	
Business	423 (32.3)	69 (30.1)	0.93	[0.69 – 1.26]
Formal employment	127 (9.7)	29 (12.7)	1.21	[0.79 – 1.86]
HIV status				
Negative	1,210 (92.3)	202 (88.2)	Ref.	
Positive	86 (6.6)	21 (9.2)	1.31	[0.83 – 2.08]
Unknown	15 (1.1)	6 (2.6)	1.82	[0.77 – 4.26]
Antenatal attendance				
No	624 (47.6)	97 (42.4)	Ref.	
Yes	687 (52.4)	132 (57.6)	1.13	[0.85 – 1.49]
History of smoking				
No	1,297 (98.9)	226 (98.7)	Ref.	
Yes	14 (1.1)	3 (1.3)	0.93	[0.29 – 2.98]
History of alcohol use				-
No	1,289 (98.3)	223 (97.4)	Ref.	
Yes	22 (1.7)	6 (2.6)	1.20	[0.52 – 2.79]
Gestational PM <sub>2.5</sub> exposure	[Mean (range)]	· ·		
PM <sub>2.5</sub> concentration	66 (45 – 75)	67 (53 – 75)	1.03	[1.01 – 1.05] **



**Quarterly Epidemiological Bulletin: July-September, 2023** 

Volume 8 / Issue 3 /Article No. 1



#### Antepartum complications

Preterm premature rupture of membranes					
No	1,223 (93.3)	213 (93.0)	Ref.		
Yes	88 (6.7)	16 (7.0)	1.24	[0.73 – 2.08]	
Hypertensive disorder					
No	1,221 (93.6)	204 (89.1)	Ref.		
Yes	84 (6.4)	25 (10.9)	1.61	[1.05 – 2.48] *	
Antepartum hemorrhag	e				
No	1,264 (96.4)	220 (96.1)	Ref.		
Yes	47 (3.6)	9 (3.9)	1.23	[0.62 – 2.43]	
Oligohydramnios					
No	1,274 (97.2)	221 (96.5)	Ref.		
Yes	37 (2.8)	8 (3.5)	1.37	[0.68 – 2.82]	
Chorioamnionitis					
No	1,271 (96.9)	222 (96.9)	Ref.		
Yes	40 (3.1)	7 (3.1)	1.06	[0.49 – 2.27]	
Intrauterine fetal death					
No	1,296 (98.9)	223 (97.4)	Ref.		
Yes	15 (1.1)	6 (2.6)	1.87	[0.81 – 4.29]	
* p<0.05 ** p<0.01	*** p<0.001				

# Association between gestational PM<sub>2.5</sub> exposure and preterm birth stratified by antepartum complications

There was a significant risk of preterm birth attributed to gestational PM<sub>2.5</sub> exposure among mothers without preterm premature rupture of membranes, hypertensive disorders, antepartum hemorrhage, oligohydramnios, chorioamnionitis, and intra uterine fetal deaths compared to those with these antepartum complications. Based on p-values, there was no statistically significant difference in stratum specific hazard ratios between gestational PM<sub>2.5</sub> exposure and incidence of preterm birth by antepartum complications (Table 3).

Antepartum complication	Frequency (%)	Stratum specific hazard ratios <sup>1</sup>	95% Confidence Intervals	p-value
Preterm premature rupture of membranes				
No	1,436 (93.2)	1.04	[1.01 – 1.06] **	
Yes	104 (6.8)	1.00	[0.93 – 1.09]	
Hypertensive disorde	r			0.564
No	1,431 (92.9)	1.03	[1.01 – 1.06] **	
Yes	109 (7.1)	1.00	[0.93 – 1.09]	
Antepartum hemorrha	age			0.511
No	1,484 (96.4)	1.03	[1.00 – 1.05] **	
Yes	56 (3.6)	1.10	[0.93 – 1.31]	
Oligohydramnios				0.897
No	1,495 (97.1)	1.03	[1.01 – 1.06] **	

# Table 3: Association between gestational PM<sub>2.5</sub> exposure and preterm birth stratified by antepartum complications, in Kampala City, Uganda, October 2021–September 2022

**Quarterly Epidemiological Bulletin: July-September, 2023** 



Volume 8 / Issue 3 /Article No. 1

Yes	45 (2.9)	1.09	[0.92 – 1.30]	0 519
Chomoannionitis				0.516
No	1,493 (97.0)	1.03	[1.01 – 1.06] **	
Yes	47 (3.0)	1.33	[0.92 – 1.93]	
Intra uterine fetal dea	ath			0.098
No	1,519 (98.6)	1.03	[1.01 – 1.06] **	
Yes	21 (1.4)	0.97	[0.87 – 1.09]	
* n < 0.05 ** n < 0.01	*** n < 0 001			

p<0.05 p<0.001

<sup>1</sup>Adjusted for age, educational level, marital status, occupation, HIV status, antenatal attendance, history of smoking and alcohol use

<sup>(e)</sup>p-values for Wald's Chi-squared test for interaction (p-values for effect modification)

# Discussion

In our assessment, gestational exposure to PM<sub>2.5</sub> concentration was considered the primary predictor of preterm birth (PTB) in Kampala City, and we subsequently adjusted for potential covariates using multivariate regression with the Cox proportional hazards model. We observed a 3% rise in the risk of PTB for each incremental unit increase in average gestational PM<sub>2.5</sub> exposure (HR=1.03, 95% CI: 1.01–1.05), after adjusting for potential covariates in our multivariate regression analysis. Notably, pregnant mothers who developed hypertensive disorders exhibited a higher likelihood of experiencing preterm births compared to their counterparts. Despite the well-established elevated risk of preterm births associated with gestational PM2.5 exposure among mothers without preterm premature rupture of membranes, hypertensive disorders, antepartum hemorrhage, oligohydramnios, chorioamnionitis, and intrauterine fetal deaths, we found that the effect modification by these antepartum complications did not achieve statistical significance.

Our findings align with previous studies which have demonstrated the increased risk of preterm births attributed to gestational PM<sub>2.5</sub> exposure. A study in Italy observed a 3% risk of preterm births per unit increase in gestational PM2.5 exposure [11]. A multi country study in Africa reported a significant association between gestational PM<sub>2.5</sub> exposure and increased risk of preterm births [1.08 (95% CI: 1.01–1.16)] [3]. A significant risk of preterm birth estimated at 1.2% per unit increase in gestational PM<sub>2.5</sub> exposure was reported based meta regression analysis across 204 countries [12]. However, inconsistent findings were reported in a retrospective cohort study among 2,966,705 million singleton live births in Canada, where gestational PM<sub>2.5</sub> exposure provided a protective effect by reducing the risk of preterm births by 20% [0.80 (95% CI: 0.75–0.86)] [13]. Another retrospective cohort study among 7,961 births occurring from June 2008 to May 2010 in Detroit, Michigan, United States revealed that maternal exposure to PM<sub>2.5</sub> was not statistically significantly associated with incidence of preterm birth (p value = 0.376) [14]. Differences in air quality, population characteristics, sample size, time periods, and PM<sub>2.5</sub> exposure measurement among studies conducted in different regions, such as Kampala, Canada and Detroit, may explain variations in the observed effects of gestational PM<sub>2.5</sub> exposure on preterm birth, with one study suggesting a protective effect while another found no significant association. Nevertheless, the significant association between gestational PM<sub>2.5</sub> exposure and preterm birth indicates the effect of air pollution on health outcomes. Such findings should implore relevant stakeholders to prioritize implementation of appropriate interventions to avert anticipated health consequences in Kampala City, where the 24-hour average PM<sub>2.5</sub> concentration from January, 2020–June, 2022, was 59 µg/m<sup>3</sup>; exceeding targeted WHO targeted safe levels [15].



Quarterly Epidemiological Bulletin: July-September, 2023



Volume 8 / Issue 3 /Article No. 1

The increased risk of preterm birth among pregnant mothers who developed hypertensive disorders has been previously evidenced. A recent scoping review highlighted hypertensive disorders among the most frequently reported risk factors for preterm births in Sub Saharan Africa [16]. A meta-analysis conducted in East African countries reported that mothers who had pregnancy induced hypertension were three times likely to experience preterm births compared to their counterparts [17]. What is quite challenging is that the risk of developing hypertensive disorders during pregnancy has also been attributed to gestational PM<sub>2.5</sub> exposure. Gestational PM<sub>2.5</sub> exposure increases the risk of pregnancy induced hypertensive disorders following endothelial dysfunction, autonomic nervous system imbalance, oxidative stress, and systemic inflammatory response [18-20]. A 5 µg/m<sup>3</sup> increment in gestational PM<sub>2.5</sub> exposure significantly increased the risk of developing pregnancy-induced hypertensive disorders by 57% [21]. Due to the complex relationship of gestational PM<sub>2.5</sub> exposure, hypertensive disorders, and preterm birth, the observed risk of preterm births among pregnant mothers who developed hypertensive disorders may as well be indirectly confounded by gestational PM<sub>2.5</sub> exposure.

Despite the growing evidence on the association between air pollution and preterm births, very few studies have investigated whether the association between gestational PM<sub>2.5</sub> exposure and birth outcomes vary by antepartum complications. We hypothesized that the effect of gestational PM<sub>2.5</sub> exposure on incidence of preterm births might be modified by antepartum complications such as preterm premature rupture of membranes, hypertensive disorders, antepartum hemorrhage, oligohydramnios, chorioamnionitis and intra uterine fetal deaths. However, this was not evidenced in this study with reference to the observed non-significant effect modification. The observed non-significant effect modification by hypertensive disorders was synonymous with findings from a population based cohort study in California which concluded that pre-existing and pregnancy-induced hypertension did not modify the relationship between air pollution and preterm birth [22]. This implies that the effect of gestational PM<sub>2.5</sub> exposure on incidence of preterm births does not differ depending on the presence or absence of the antepartum complication.

#### Study strengths and limitations

Our findings should be interpreted in line with the following limitation. We were unable to reach out to 1,354 mothers who met the eligibility criteria because they did not have valid documented telephone contacts. We were not able to confirm their primary address and thus excluded them from the analysis. This could have led to underestimation or over estimation of the risk of preterm births attributed to gestational PM<sub>2.5</sub> exposure in Kampala City. Despite the limitation, this assessment presents the first comprehensive investigation examining the association between gestational PM<sub>2.5</sub> exposure and preterm birth in Kampala City using ground-level air quality data sourced from Clarity© Node Solar-Powered low-cost monitors.

#### Conclusion

We observed a significant impact of air pollution on the incidence of preterm births in Kampala City. Kampala Capital City Authority and other relevant partners are implored to prioritize interventions aimed at reducing air pollution to improve maternal and child health. Furthermore, efforts aimed at reducing preterm births should not underscore the urgent need to mitigate air pollution.



Quarterly Epidemiological Bulletin: July-September, 2023

Volume 8 / Issue 3 /Article No. 1



### **Conflict of interest**

The authors declare no conflict of interest.

#### Authors' contributions

MN designed the protocol under the technical guidance of AN, AO, SZ, DA, TK, PW, LA, DK, LB, RM, ARA, LA, JRH, and DAO. MN, AN, DA, TK and SZ supervised data collection, analyzed, and interpreted the data. MN drafted the bulletin. MN, AN, AO, PW, LA, DK, LB, RM, ARA, LA, JRH, and DAO, critically reviewed the bulletin for intellectual content. All co–authors read and approved the final bulletin.

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